(9)

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,571	12/27/2001	Shuyuan Zhang	29853/37702	9714

7590 10/21/2004

JEFFREY S. SHARP
MARSHALL, GERSTEIN & BORUN
6300 SEARS TOWER
233 SOUTH WACKER DRIVE
CHICAGO, IL 60606-6357

EXAMINER	
MOSHER, MARY	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/033,571	ZHANG ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-128* is/are pending in the application.

4a) Of the above claim(s) *99-128* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-98* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/3/02, 9/15/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Inventorship

In view of the papers filed 5/15/2003, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by addition of Deborah Wilson and Lucetta Caston.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Election/Restrictions

Applicant's election without traverse of group I, claims 70-98 in the reply filed on 6/23/3004 is acknowledged.

Claims 99-128 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/23/2004.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 70-98 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-89 of U.S. Patent No. 6,194,191. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of purifying adenovirus involving steps of providing nutrients to adenovirus-infected cells, lysing the cells, and purifying the virus. The patented claims recite a variety of combinations of elements for nutrient provision, methods of lysing, and methods of purifying. The instant claims are still another combination of the same elements that are recited in different combinations in the patented claims. Furthermore, instant claim 70 fully encompasses the subject matter of previously patented claim 86.

Claim Rejections - 35 USC § 112

Claims 70-98 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All of these claims are drawn to a process of making an adenovirus composition "for therapeutic use." In claims 97 and 98 particularly, the invention is defined chiefly by a "chromatography step capable of providing a purified adenovirus composition for therapeutic use." However, it is not clear from the specification what characteristics make an adenovirus composition suitable "for therapeutic use", and it is not clear where the line lies which distinguishes between a

composition "for therapeutic use" and a composition unsuitable for that intended use. Since the metes and bounds of "therapeutic" compositions are undefined, it is not clear what the chromatography step must accomplish to be "capable of providing a purified adenovirus composition for therapeutic use." This, in turn, renders the claim unclear in what processes are encompassed by the claims. Although this lack of clarity is most easily recognized in claims 97 and 98, claims 70-97 also require the end product to be suitable "for therapeutic use," and therefore involve the same uncertainty.

In addition, for claim 72, it is not clear what constitutes "a substantially purified adenovirus composition", nor clear what active steps are required to obtain this end product.

Claims 73-78, 94-96 are also rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active steps that produce the end product with the characteristics recited in the claim. The parent claim 70 is very broadly drawn to a process of growing cells (fed in a specified manner), infecting the cells with adenovirus, lysing them, and purifying the adenovirus by any method other than CsCl centrifugation. Dependent claims 73-78, 94-96 recite the wished-for characteristics of the end product, but do not recite any active steps that are responsible for producing these wished-for characteristics. Since it is not clear what steps produce the products recited in these claims, the claims are seen as incomplete.

Claims 70-98 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to methods of purifying adenoviruses to a degree of purity suitable for use in therapeutic compositions. Dependent claims 73-78, 95-96 recite specific desired characteristics of the purified product. The claims do not state the active steps used to obtain the desired pure product (other than excluding CsCl density gradient centrifugation, and in claims 98-99 requiring a chromatography step). The claims are therefore drawn to a genus of methods. At the time the invention was made, there was a wide choice of purification methods available in the biotechnology art, and widespread recognition that the effect of any procedure on product yield and quality was difficult to predict in the absence of empirical testing. The specification teaches reduction to practice of one series of steps which results in highly purified product with the characteristics recited in,., for example, claims 73-78. The specification provides general guidance that strong anionic exchange chromatography is superior to other modes of chromatography (see page 94 for example), but provides very limited guidance as to other forms of purification that would achieve the desired goal. Contrasting the limited species reduced to practice versus the broad scope of the methods as generically claimed, and considering the unpredictability of the purification art, it is concluded that the specification does not reasonably communicate that applicants possessed the full range of methods embraced by the generic claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 70, 72, 73, 75-77, 80-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shabram et al 5,837,520 in view of Perrin et al (Vaccine 13(13):1244-1250, 1995), Garnier et al (Cytotechnology 15:145-155, 1994), and/or Nadeau et al (Biotechnology and Bioengineering 51:613-623, 1996). Shabram describes a method for producing an adenovirus comprising harvesting and lysing cells, reducing the concentration of contaminating nucleic acids with Benzonase, and isolating the virus with any of a variety of chromatographic media, including anion exchange chromatography. Shabram teaches products with the 260/280 ratios recited in claims 75-76, and, considering that the products appear to be at least as pure as CsCl-gradient virus, the products are reasonably believed to meet the requirements of claims 73 and

77. Shabram differs from the claimed invention in that the host cells were grown in batch mode, not perfused during growth. However, in the art of virus production, perfusion cultures have been used for large-scale growth of cells for virus production, for example by Perrin et al, and Garnier et al and Nadeau et al teach scale-up of adenovirus growth using medium replacement and fed-batch conditions controlling the glucose concentration for improved yield. It would have been within the ordinary skill of the art to scale up culture using a perfusion system, for the advantages of large-scale production of virus as suggested by Perrin et al, and to optimize the rate of medium replacement and glucose level for the advantage of improving yield as taught for adenovirus by Garner et al and Nadeau et al. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Claims 78, 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shabram et al in view of Perrin et al, Garner et al, and/or Nadeau et al as applied to claims 70, 72, 73, 75-77, 80-97 above, and further in view of Morris et al (Williamsburg BioProcessing Conference, Nov. 18-21, 1996) or Gilbert (Williamsburg BioProcessing Conference, Nov. 18-21, 1996). These claims differ from the above in requiring serum-free media, or a serum-free product. Cells adapted to serum-free medium have been used for large scale production of viruses, see for example Perrin et al, for the purposes of inexpensive scale up. Morris et al and Gilbert specifically teach production of adenovirus in cells adapted to serum-free media. It therefore would have been obvious to further use cells adapted to serum-free media, for the purposes of reduced expense,

resulting in a product without detectable serum contamination. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Information Disclosure Statement

In the Information Disclosure Statement filed 6/3/2002, the Japanese patent and the Search Report have not been considered, as these do not appear to have been made of record in the parent application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600

10/18/04